

## New Mechanism of "Dead Zone" Formation in Large Arteries (According to a New Theory of Cardiovascular Disease)

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### ABSTRACT

**Background:** Arterial dead zone (ADZ) is a serious medical problem. It has been argued that violations in the work of the heart cause various pathological processes that lead to the development of a dead zone.

In accordance with the new mechanism of DZ development, the main cause of DZ formation is changes in the arterial wall, which lead to disruption of its contractile function. It is the formation of DZ in large and medium-sized arteries that causes the development of severe pathological changes leading to the development of such diseases as myocardial infarction, stroke, and aneurysm.

### Keywords

Large arteries, Dead Zone (DZ), New mechanism, Cardiovascular disease.

### Rationale

According to calculations - the length of the arterial bed is 29.1-504,6 km. Mathematical modeling showed that if the delivery of blood from the heart to the capillary bed, the required power ranges from 660 to 11942 W. Thus, the main load during transportation the blood to the capillary bed rests on the artery but not on the heart and the vascular pump plays the major role in transportation of blood. Even minor changes in the wall of the arteries, which disrupts vascular pump, lead to the emergence of various vascular diseases. The rationale for this idea I got Ming Chien Kao Awards 2015.

It is disorders in the vascular pump that lead to the formation of DZ. The DZ formation in arteries leads to ischemia, heart attacks, strokes, and gangrene. Previously, it was believed that DZ is formed due to atherosclerosis, embolism and other diseases leading to partial or complete occlusion of the blood vessel. We have confirmed another mechanism of DZ formation. Changes in the arterial wall, which lead to a violation of its contractile function are the main cause of DZ formation. Only then do ischemic,

atherosclerotic, inflammatory, and other changes appear.

### Introduction

Cardiovascular disease remains the leading cause of death worldwide despite effective interventions [1]. For example, hypertension continues to be a significant yet preventable risk factor for cardiovascular disease events, contributing to 55% of deaths related to ischemic heart disease and 45% of deaths related to cerebrovascular disease [2]. Multiple studies have shown that the main cause of DZ development is various pathological changes. It is these changes that lead to DZ formation (atherosclerosis [3,4], thrombosis and embolism [5,6], arterial spasm [7,8], vasculitis and inflammatory diseases [9,10], diabetes and metabolic disorders [11,12], hypertension [13,14].

Our research has contradicted this opinion. The main role in the development of all cardiovascular diseases is attributed to the disruption of arteries transporting blood to organs. These or those diseases will occur depending on where the dead zone is formed in the arteries supplying blood to one or another organ [15-20].

### Mechanism of Dead Zone Formation (DZ)

A comparison of the clinical results of using constant and frequency intravenous blood irradiation has shown that frequency irradiation,

with all the same parameters, reduces blood pressure to a greater extent. This is the result of a vascular bed response rather than a reduction in cardiac output [21,22].

From the point of view of the mechanics, it is impossible to explain how at the average power of the heart in rest - 3,3 W [23-25] the heart can pump the blood through the vascular system which length makes about 100 thousand kilometers. Although according to well-known authors, mainly in the transportation of blood was heart [26-28].

It was not explained how blood is delivered to organs and tissues with such a small cardiac output capacity and huge length of arteries. It has turned out that different types of arteries have different anatomical structures [23,24,26]. It became evident that only due to the work of muscular-elastic pump of arteries blood is delivered to tissues. On these grounds, our studies proved a new principle of the work of the cardiovascular system and a new theory of the development of cardiovascular diseases [15-19].

Mathematical research proved that power from 660W to 11942 W is required to deliver blood to tissues and organs [20,21].

It is segmental arterial dysfunctions that lead to the dead zone (DZ) formation. In large and medium-sized arteries, the WZ triggers the development of severe pathological changes in the arterial wall, such as coronary thrombosis, atherosclerosis, violation of blood transportation on the affected area, etc. These processes bring about the development of such diseases as myocardial infarction, stroke, aneurysm.

### How DZ Formation has an Impact on Impaired Blood Flow in Elastic and Musculo-elastic Arteries

The presented schemes of blood flow in these types of arteries illustrate more clearly how DZ formation affects blood flow.

**Elastic type** (aorta, pulmonary trunk, pulmonary, common carotid artery) consists of two shells (only elastic frame)- performs the function of a compression chamber, expanding during systole and tapering during diastole. There are baroreceptors that respond to mechanical stretching Diagram of blood flow in Elastic types of arteries (Figure 1).

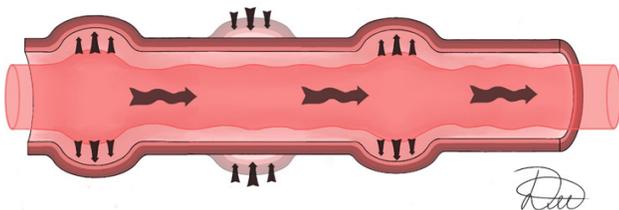
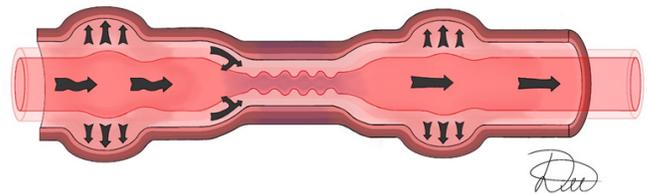


Diagram of blood flow in Elastic type of arteries when forming a DZ (Figure 2).

The arteries of the elastic type of work as a compression chamber. It does not contain spiral-shaped muscle fibers, the contraction of

which provide a progressive laminar blood flow. Blood flow is formed due to increased pressure from the upper parts and wave-like transverse contraction of elastic fibers of the vascular wall. The formation of DZ primarily disrupts the contractile function of the arterial wall, and the formation of the return wave significantly increases the shear stress. Due to the formation of the return wave and increased shear stress, pulse dilatation of the artery is disturbed. All these changes cause dysfunction of all layers of the vascular wall both in the DZ zone and above the affected area.



**Elastic and muscular type** (subclavian, external and internal iliac, femoral, mesenteric artery, celiac trunk) - joins the muscular layer (spiral arrangement of fibers). This arrangement of fibers while reducing the flow makes blood spiral. The baroreceptors disappear and sympathetic adrenergic vasoconstrictor fibers appear. Diagram of blood flow in Elastic and muscular type (Figure 3).

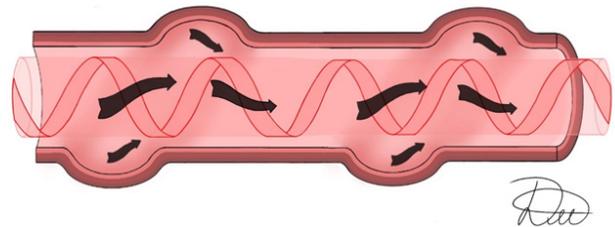
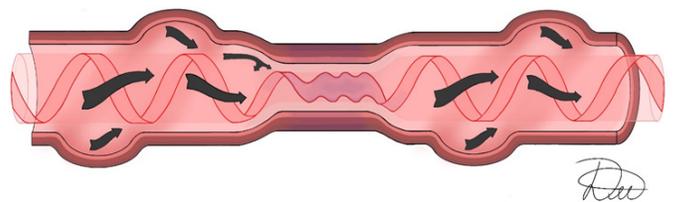


Diagram of blood flow in Elastic and muscular type of arteries when forming a DZ (Figure 4).



Spiral-shaped muscle fibers appear in the elastic-muscular type of arteries. The wave-like contraction of these fibers makes the laminar flow spiral. This increases the contractile function of the wall and reduces the shear stress of the blood vessel.

DZ formation disrupts blood flow to a lesser extent. In the affected area and above, due to synchronous contraction of elastic and muscle fibers, laminar spiral blood flow is restored.

DZ formation primarily violates the contractile function of the arterial wall, while the return wave significantly increases the

shear stress. As the elastic-muscular framework appears, the disturbances of pulse dilatation and arterial remodeling are less distinct. All these changes provoke disturbance of the function of all layers of the vascular wall both in the DZ, and above the affected area. Below the DZ, laminar spiral blood flow returns to its normal state.

### DZ as a Trigger for the Formation of Severe Vascular Disease

The formation of DZ is individual in nature. It can be a long-term process, when there is a steady disruption of the contractile function of the artery, followed by complete blockage of blood flow in the affected area. It can also be a very rapid process when these changes occur within a short time. Everything depends on those pathological changes (metabolic, hormonal, inflammatory and neurological, etc.) that affect the formation of DZ. Regardless of the etiology of DZ formation, it triggers a set of pathological changes that give rise to such severe pathology as heart attack, stroke, aneurysm, bursting of the vessel wall. How DZ formation affects the origin of these diseases is presented in Scheme 1.

Thus, the formation of DZ in large arteries triggers avalanche-like pathological changes in the vessel wall, which lead to the most severe coronary pathology, which holds the first place in terms of mortality in the world.

### Discussion

There is no a consensus on what factors influence DZ formation. Some authors suggest that the root cause of DZ formation is various pathological processes (atherosclerosis [3,4], thrombosis and embolism [5,6], arterial spasm [7,8], vasculitis and inflammatory diseases [9,10], diabetes mellitus and metabolic disorders [11,12], hypertension [13,14].

Other authors argue that the main contribution is made by biomechanical disorders in arteries, which are the trigger mechanism of pathological changes (atherosclerosis [29-33], low-density lipoprotein metabolism disorders [34-38], endothelial dysfunction and inflammation [39-43], vascular permeability disorders [44-56], thrombosis [57].

At the same time, other researchers have suggested that pathological changes in the arterial wall, may drive the development of various pathological processes.

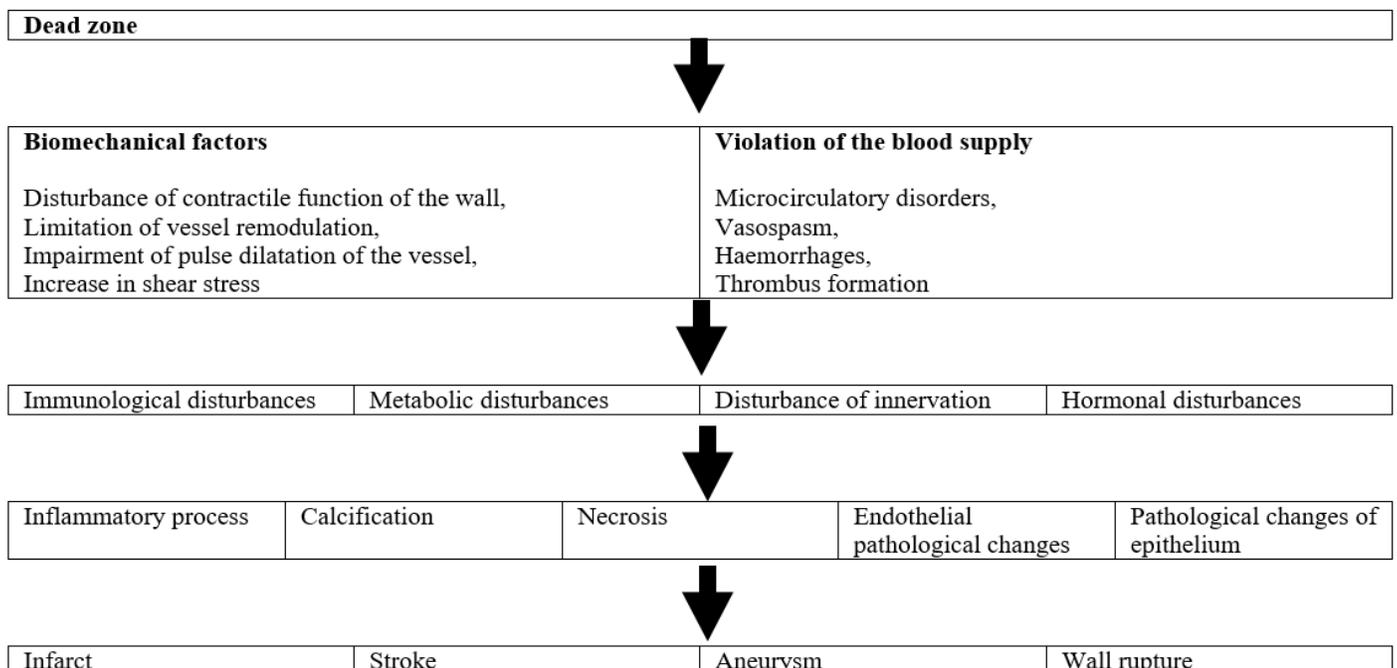
This has been confirmed by morphological studies of coronary arteries. They showed that accumulation of monocytes, lipids and in the subepithelial space leads to inflammatory and atherosclerotic changes in smooth muscle [58,59].

Haverich A, on the basis of hundreds of cardiovascular operations performed, suggested that vasa vasorum occlusion, is an early major pathophysiological mechanism that triggers the development of inflammation from the adventitia to the intima [60].

Hormonal disturbances are also stimulators of inflammation in smooth muscle and epithelial cells [61-77].

The problem was viewed from the perspective that cardiac dysfunction leads to biomechanical abnormalities in the arteries.

Only when a new principle of cardiovascular system operation and a new theory of cardiovascular disease development were proved, it became clear that the trigger mechanism of DZ development is pathological changes in the arterial wall. It is pathological changes in the arterial wall that first lead to biomechanical disturbances in the affected area, with subsequent development of a whole chain of pathological processes.



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## Conclusion

1. According to the new principle of the cardiovascular system, it is precisely segmental disorders in the arteries that lead to the formation of 'dead zone' (DZ).
2. The formation of DZ avalanche-like causes the development of pathological processes, both in the affected area and above the level of the damage, especially in arteries of elastic type.
3. DZ formation in large arteries results in pathological changes that lead to severe coronary pathology such as heart attack, stroke, aneurysm, rupture of the arterial wall.

## References

1. <https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases>
2. Husain MJ, Datta BK, Kostova D, et al. Access to cardiovascular disease and hypertension medicines in developing countries: an analysis of essential medicine lists, price, availability, and affordability. *JAHA*. 2020; 9: e015302.
3. Libby P, Ridker PM, Hansson GK, et al. Inflammation in Atherosclerosis: From Pathophysiology to Practice. *J Am Coll Cardiol*. 2009; 54: 2129-2138.
4. Ross R. Atherosclerosis - An Inflammatory Disease. *N Engl J Med*. 1999; 340: 115-126.
5. Virchow R. Thrombosis and Embolism: The Triad of Factors.
6. Heit J.A. Epidemiology of Venous Thromboembolism. *Nat Rev Cardiol*. 2015; 12: 464-474.
7. Lüscher TF, Vanhoutte PM. The Endothelium: Modulator of Cardiovascular Function. CRC Press. 1990; 228.
8. Hirofumi Yasue, Hitoshi Nakagawa, Teruhiko Itoh, et al. Coronary Artery Spasm: Clinical Features, Diagnosis, Pathogenesis, and Treatment. *J Cardiol*. 2008; 51: 2-17.
9. Jennette JC, Falk RJ. Pathogenesis of Antineutrophil Cytoplasmic Autoantibody-Mediated Vasculitis. *Nat Rev Rheumatol*. 2014; 10: 463-473.
10. G S Kerr, C W Hallahan, J Giordano, et al. Takayasu Arteritis. *Ann Intern Med*. 1994; 120: 919-929.
11. Brownlee M. Biochemistry and Molecular Cell Biology of Diabetic Complications. *Nature*. 2001; 414: 813-820.
12. Josephine M Forbes, Mark E Cooper. Mechanisms of Diabetic Complications. *Physiol Rev*. 2013; 93: 137-188.
13. Aram V. Chobanian, George L. Bakris, Henry R. Black, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003; 289: 2560-2571.
14. Michel E Safar, Bernard I Levy, Harry Struijker-Boudier. Current Perspectives on Arterial Stiffness and Pulse Pressure in Hypertension and Cardiovascular Diseases. *Circulation*. 2003; 107: 2864-2869.
15. Mikhaylov VA. Newly discovered way of the function of cardio-vascular System and the latest theory of the development of cardio-Vascular diseases. Abstr. International conference surgery. Toronto, Canada. 2017.
16. Mikhaylov VA. Newly discovered way of the function of cardio-vascular system and the latest theory of the development of Hypertension and other cardio-vascular diseases. *EC Cardiology*. 2017; 5: 179-187.
17. Mikhaylov VA. Newly discovered way of the function of cardio-vascular system and the latest theory of the development of Hypertension and other cardio-vascular diseases. EuroSciCon Conference on Clinical Cardiology and Cardiovascular Disease. London, UK. 2018.
18. Mikhaylov VA. Newly discovered way of the function of cardio-vascular system and the latest theory of the development of Hypertension and other cardio-vascular diseases. Global Conference on Cardiology. Rome, Italy. 2019.
19. Vladimir A. Mikhaylov, Tatiana Y. Mikhaylova. Anatomical-physiological and mathematical justification of the new principle of the function of the cardiovascular system and the development of cardiovascular diseases. International Conference on Clinical and Medical Case Reports. 2019.
20. Mikhaylov VA, Mikhaylova TY. Anatomical-Physiological And Mathematical Justification Of The New Principle Of The Function Of The Cardiovascular System And The Development Of Cardiovascular Diseases. International Journal of Hematology and Blood Research. 2019; 1: 10-15.
21. Mikhaylov VA. Use of intravenous laser blood irradiation (ILBI) at 630-640 nm to prevent vascular diseases and to increase life expectancy. *Laser Therapy*. 2015; 24: 15-26.
22. Mikhaylov VA. Ming Chien Kao Awards 2015. *Laser Therapy*. 2016; 25: 9-10.
23. McDonald DA. Blood Flow in Arteries. 2nd Ed. London. Arnold. 1974.
24. Guyton AC, Young DB. Cardiovascular Physiology III, Vol.18., Baltimore. University Park Press. 1979.
25. Ilyich GK. Medical and biological physics: fluctuations and waves, acoustics, hemodynamics Minsk. 2000.
26. Shepherd JT, Abboud FM. Handbook of Physiology, Section 2. The Cardiovascular System. Vol. III. Peripheral Circulation and Organ Blood Flow. Bethesda. Marulend. American Physiological Society. 1983.
27. Schmidt RF, Thews G. Human Physiology. London Paris Tokio Hong Kong. 1996.
28. Parashin VB, Itkin GP. Biomechanic circulation. Moscow, State University named N. Uh. Bauman. 2005.
29. Brenda R Kwak, Magnus Bäck, Marie-Luce Bochaton-Piallat, et al. Biomechanical factors in atherosclerosis: Mechanisms and clinical implications. *Eur Heart J*. 2014; 35: 3013-3020.
30. Malek AM, Alper S, Izumo S. Hemodynamic shear stress and its role in at herosclerosis. *JAMA*. 1999; 282: 2035-2042.
31. Back M, Gasser T, Michel JB, et al. Biomechanical factors in the biology of aortic wall and aortic valve diseases. *Cardiovasc Res*. 2013; 99: 232-241.
32. Cheng C, Tempel D, Van Haperen R, et al. Atherosclerotic lesion size and vulnerability are determined by patterns of fluid shear stress. *Circulation*. 2006; 113: 2744-2753.

33. Caroline Cheng, Rien van Haperen, Monique de Waard, et al. Shear stress affects the intracellular distribution of eNOS: direct demonstration by a novel in vivo technique. *Blood*. 2005; 106: 3691-3698.
34. Foteinos G, Hu YH, Xiao QZ, et al. Rapid endothelial turnover in atherosclerosis-prone areas coincides with stem cell repair in apolipoprotein E-deficient mice. *Circulation*. 2008; 117: 1856-1863.
35. Schober A, Nazari-Jahantigh M, Wei Y, et al. MicroRNA-126-5p promotes endothelial proliferation and limits atherosclerosis by suppressing Dlk1. *Nat Med*. 2014; 20: 368-376.
36. Chaudhury H, Zakkar M, Boyle J, et al. c-Jun N-terminal kinase primes endothelial cells at atheroprone sites for apoptosis. *Arterioscler Thromb Vasc Biol*. 2010; 30: 546-553.
37. Hansson GK, Chao S, Schwartz SM, et al. Aortic endothelial-cell death and replication in normal and lipopolysaccharide-treated rats. *Am J Pathol*. 1985; 121: 123-127.
38. Varnava AM, Mills PG, Davies MJ. Relationship between coronary artery remodeling and plaque vulnerability. *Circulation*. 2002; 105: 939-943.
39. Steinman DA. Simulated pathline visualization of computed periodic blood flow patterns. *J Biomech*. 2000; 33: 623-628.
40. Li S, Butler P, Wang YX, et al. The role of the dynamics of focal adhesion kinase in the mechanotaxis of endothelial cells. *Proc Natl Acad Sci USA*. 2002; 99: 3546-3551.
41. Haga J, Li Y-SJ, Chien S. Molecular basis of the effects of mechanical stretch on vascular smooth muscle cells. *J Biomech*. 2007; 40: 947-960.
42. Shyu KG. Cellular and molecular effects of mechanical stretch on vascular cells and cardiac myocytes. *Clin Sci*. 2009; 116: 377-389.
43. Chaabane C, Otsuka F, Virmani R, et al. Biological responses in stented arteries. *Cardiovasc Res*. 2013; 99: 353-363.
44. Jo H, Dull RO, Hollis TM, et al. Endothelial albumin permeability is shear dependent, time-dependent, and reversible. *Am J Physiol*. 1991; 260: 1992-1996.
45. Davies PF. Endothelial mechanisms of flow-mediated atheroprotection and susceptibility. *Circ Res*. 2007; 101: 10-12.
46. Suo J, Ferrara DE, Sorescu D, et al. Hemodynamic shear stresses in mouse aortas-implications for atherogenesis. *Arterioscler Thromb Vasc Biol*. 2007; 27: 346-351.
47. Dai GH, Kaazempur-Mofrad MR, Natarajan S, et al. Distinct endothelial phenotypes evoked by arterial waveforms derived from atherosclerosis-susceptible and-resistant regions of human vasculature. *Proc Natl Acad Sci USA*. 2004; 101: 14871-14876.
48. Foteinos G, Hu YH, Xiao QZ, et al. Rapid endothelial turnover in atherosclerosis-prone areas coincides with stem cell repair in apolipoprotein E-deficient mice. *Circulation*. 2008; 117: 1856-1863.
49. Zeng LF, Zampetaki A, Margariti A, et al. Sustained activation of XBP1 splicing leads to endothelial apoptosis and atherosclerosis development in response to disturbed flow. *Proc Natl Acad Sci USA*. 2009; 106: 8326-8331.
50. Hajra L, Evans AI, Chen M, et al. The NF-kappa B signal transduction pathway in aortic endothelial cells is primed for activation in regions predisposed to atherosclerotic lesion formation. *Proc Natl Acad Sci U S A*. 2000; 97: 9052-9057.
51. Cuhlmann S, Van der Heiden K, Saliba D, et al. Disturbed blood flow induces RelA expression via c-Jun N-terminal kinase 1 A novel mode of NF-kappa B regulation that promotes arterial inflammation. *Circ Res*. 2011; 108: 950-959.
52. Zakkar M, Chaudhury H, Sandvik G, et al. Increased endothelial mitogenactivated protein kinase phosphatase-1 expression suppresses proinflammatory activation at sites that are resistant to atherosclerosis. *Circ Res*. 2008; 103: 726-732.
53. Passerini AG, Polacek DC, Shi CZ, et al. Coexisting proinflammatory and antioxidative endothelial transcription profiles in a disturbed flow region of the adult porcine aorta. *Proc Natl Acad Sci USA*. 2004; 101: 2482-2487.
54. Civelek M, Manduchi E, Riley RJ, et al. Chronic endoplasmic reticulum stress activates unfolded protein response in arterial endothelium in regions of susceptibility to atherosclerosis. *Circ Res*. 2009; 105: 453-461.
55. Magid R, Davies PF. Endothelial protein kinase C isoform identity and differential activity of PKC xi in an atherosusceptible region of porcine aorta. *Circ Res*. 2005; 97: 443-449.
56. Schober A, Nazari-Jahantigh M, Wei Y, et al. MicroRNA-126-5p promotes endothelial proliferation and limits atherosclerosis by suppressing Dlk1. *Nat Med*. 2014; 20: 368-376.
57. Frueh J, Maimari N, Homma T, et al. Systems biology of the functional and dysfunctional endothelium. *Cardiovasc Res*. 2013; 99: 334-341.
58. Nakashima Y, Wight TN, Sueishi K. Early atherosclerosis in humans: role of diffuse intimal thickening and extracellular matrix proteoglycans. *Cardiovasc Res*. 2008; 79: 14-23.
59. Moore KJ, Tabas I. Macrophages in the pathogenesis of atherosclerosis. *Cell*. 2011; 145: 341-355.
60. Haverich A. A surgeon's view on the pathogenesis of atherosclerosis. *Circulation*. 2017; 135: 205-207.
61. Anaïs Yerly, Emiel P C van der Vorst, Iris Baumgartner, et al. Sex-specific and hormone-related differences in vascular remodelling in atherosclerosis. *Eur J Clin Invest*. 2023; 53: e13885.
62. Arenas IA, Armstrong SJ, Xu Y, et al. Chronic tumor necrosis factor-alpha inhibition enhances NO modulation of vascular function in estrogen-deficient rats. *Hypertension*. 2005; 46: 76-81.
63. Miller AP, Feng W, Xing D, et al. Estrogen modulates inflammatory mediator expression and neutrophil chemotaxis in injured arteries. *Circulation*. 2004; 110: 1664-1669.
64. Evans BR, Yerly A, van der Vorst EPC, et al. Inflammatory mediators in atherosclerotic vascular remodeling. *Front Cardiovasc Med*. 2022; 9: 868934.

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65. Xing D, Miller A, Novak L, et al. Estradiol and progestins differentially modulate leukocyte infiltration after vascular injury. *Circulation*. 2004; 109: 234-241.
  66. Savolainen-Peltonen H, Loubtchenkov M, Petrov L, et al. Estrogen regulates insulin-like growth factor 1, platelet-derived growth factor a and B, and their receptors in the vascular wall. *Transplantation*. 2004; 77: 35-42.
  67. Liu SL, Bajpai A, Hawthorne EA, et al. Cardiovascular protection in females linked to estrogen-dependent inhibition of arterial stiffening and macrophage MMP12. *JCI Insight*. 2019; 4: e122742.
  68. Cavin MA, Tao ZY, Yu AL, et al. Testosterone enhances early cardiac remodeling after myocardial infarction, causing rupture and degrading cardiac function. *Am J Physiol Heart Circ Physiol*. 2006; 290: 2043-2050.
  69. Fairweather D. Sex differences in inflammation during atherosclerosis. *Clin Med Insights Cardiol*. 2014; 8: 49-59.
  70. Huang CK, Pang H, Wang L, et al. New therapy via targeting androgen receptor in monocytes/macrophages to battle atherosclerosis. *Hypertension*. 2014; 63: 1345-1353.
  71. Wang M, Tsai BM, Kher A, et al. Role of endogenous testosterone in myocardial proinflammatory and proapoptotic signaling after acute ischemia-reperfusion. *Am J Physiol Heart Circ Physiol*. 2005; 288: 221-226.
  72. Bernardi S, Toffoli B, Tonon F, et al. Sex differences in proatherogenic cytokine levels. *Int J Mol Sci*. 2020; 21: 3861.
  73. Traish A, Bolanos J, Nair S, et al. Do androgens modulate the pathophysiological pathways of inflammation? Appraising the contemporary evidence. *J Clin Med*. 2018; 7: 549.
  74. Malkin CJ, Pugh PJ, Jones RD, et al. The effect of testosterone replacement on endogenous inflammatory cytokines and lipid profiles in hypogonadal men. *J Clin Endocrinol Metab*. 2004; 89: 3313-3318.
  75. Sergi D, Campbell FM, Grant C, et al. SerpinA3N is a novel hypothalamic gene upregulated by a high-fat diet and leptin in mice. *Genes Nutr*. 2018; 13: 28.
  76. Lubos E, Schnabel R, Rupprecht HJ, et al. Prognostic value of tissue inhibitor of metalloproteinase-1 for cardiovascular death among patients with cardiovascular disease: results from the AtheroGene study. *Eur Heart J*. 2006; 27: 150-156.
  77. Coronado MJ, Brandt JE, Kim E, et al. Testosterone and interleukin-1beta increase cardiac remodeling during coxsackievirus B3 myocarditis via serpin a 3n. *Am J Physiol Heart Circ Physiol*. 2012; 302: 1726-1736.